

ANTIHYPERTENSIVES

BY

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**Treatment does not bring back
the risk to that of someone
without hypertension,.. High
blood pressure raises the risk
threefold and treatment reduces
it by 25%**

Walter Willet

G O A L S

SHORT TERM

Reduce blood pressure.



VS,

LONG TERM

Reduce cardiovascular and renal morbidity and mortality





Strategies

Mild hypertension can sometimes be controlled with a single drug, but most patients require more than one drug to achieve blood pressure control

Current

Recommendations

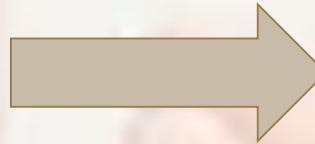
Initiate therapy with a thiazide diuretic unless there are compelling reasons to employ other drug classes



- If blood pressure is inadequately controlled, a second drug is added, with the selection based on minimizing the adverse effects of the combined regimen and achieving goal blood pressure.

PATIENT COMPLIANCE

Lack of patient compliance is the most common reason for failure of antihypertensive therapy



The adverse effects associated with the hypertensive therapy may influence the patient more than the future benefits.



Thus, it is important to enhance compliance by carefully selecting a drug regimen that both reduces adverse effects and minimizes the number of doses required daily.

INDIVIDUALIZED CARE

Certain subsets of the hypertensive population respond better to one class of drug than they do to another



For Example:

calcium-channel blockers, ACE inhibitors, and diuretics are favored for treatment of hypertension in elderly patients, whereas β -blockers and α -antagonists are less well tolerated.

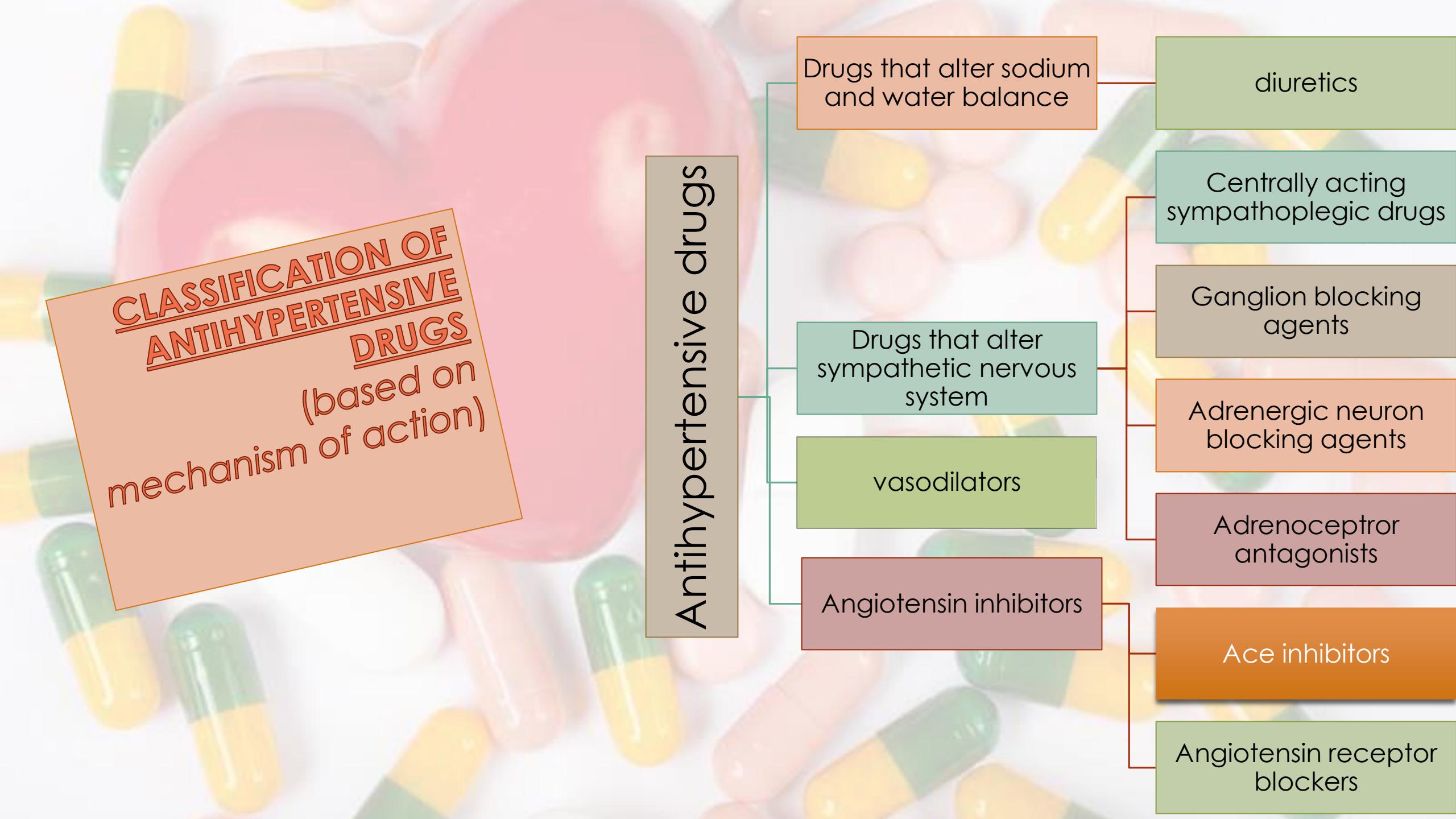
Hypertension may coexist with other diseases that can be aggravated by some of the antihypertensive drugs



In such cases, it is important to match antihypertensive drugs to the particular patient.



Antihypertensives



CLASSIFICATION OF ANTIHYPERTENSIVE DRUGS (based on mechanism of action)

Antihypertensive drugs

Drugs that alter sodium and water balance

diuretics

Drugs that alter sympathetic nervous system

Centrally acting sympathoplegic drugs

vasodilators

Ganglion blocking agents

Angiotensin inhibitors

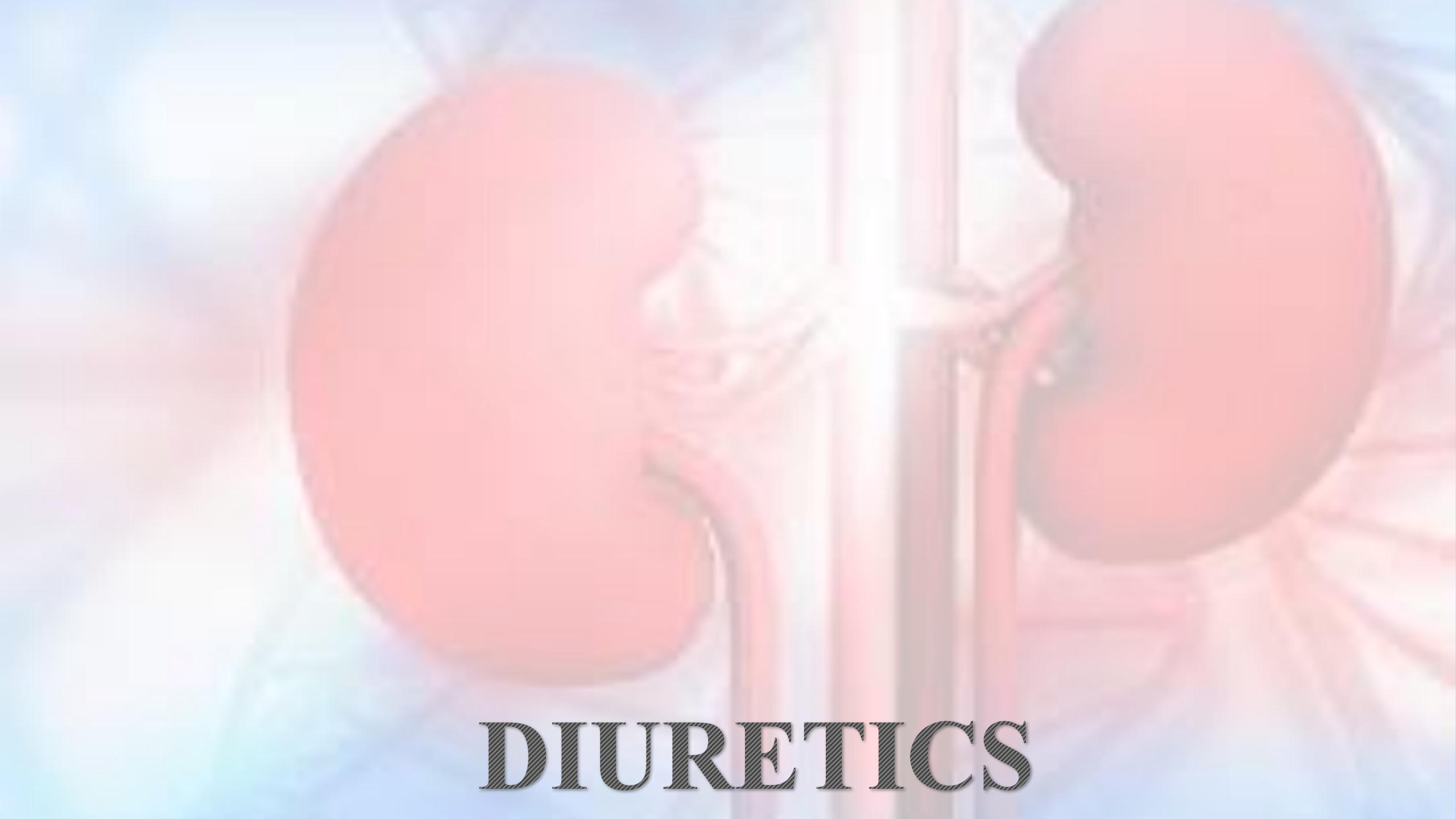
Adrenergic neuron blocking agents

Adrenoceptor antagonists

Ace inhibitors

Angiotensin receptor blockers

DRUGS THAT ALTER SODIUM WATER BALANCE

A blurry background photograph of a person sitting on a bench, looking down at their phone. The person is wearing a light-colored shirt and dark pants. The background is a soft-focus outdoor scene.

DIURETICS

OVERVIEW

Diuretics can be used as first-line drug therapy for hypertension unless there are compelling reasons to choose another agent.

Reduce blood pressure by reducing blood volume and cardiac output

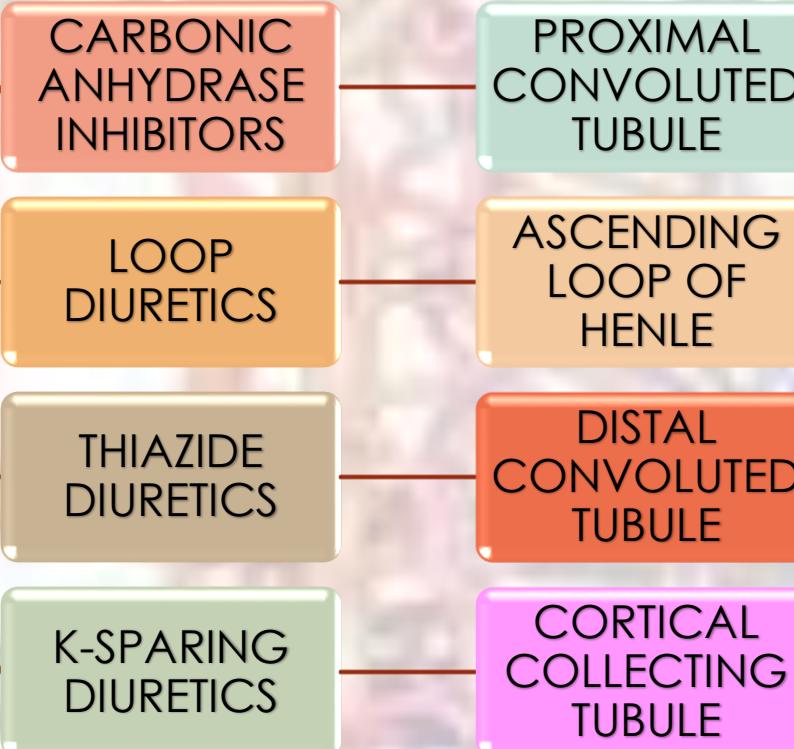
Effective in lowering b.p by 10-15mmhg in most patients

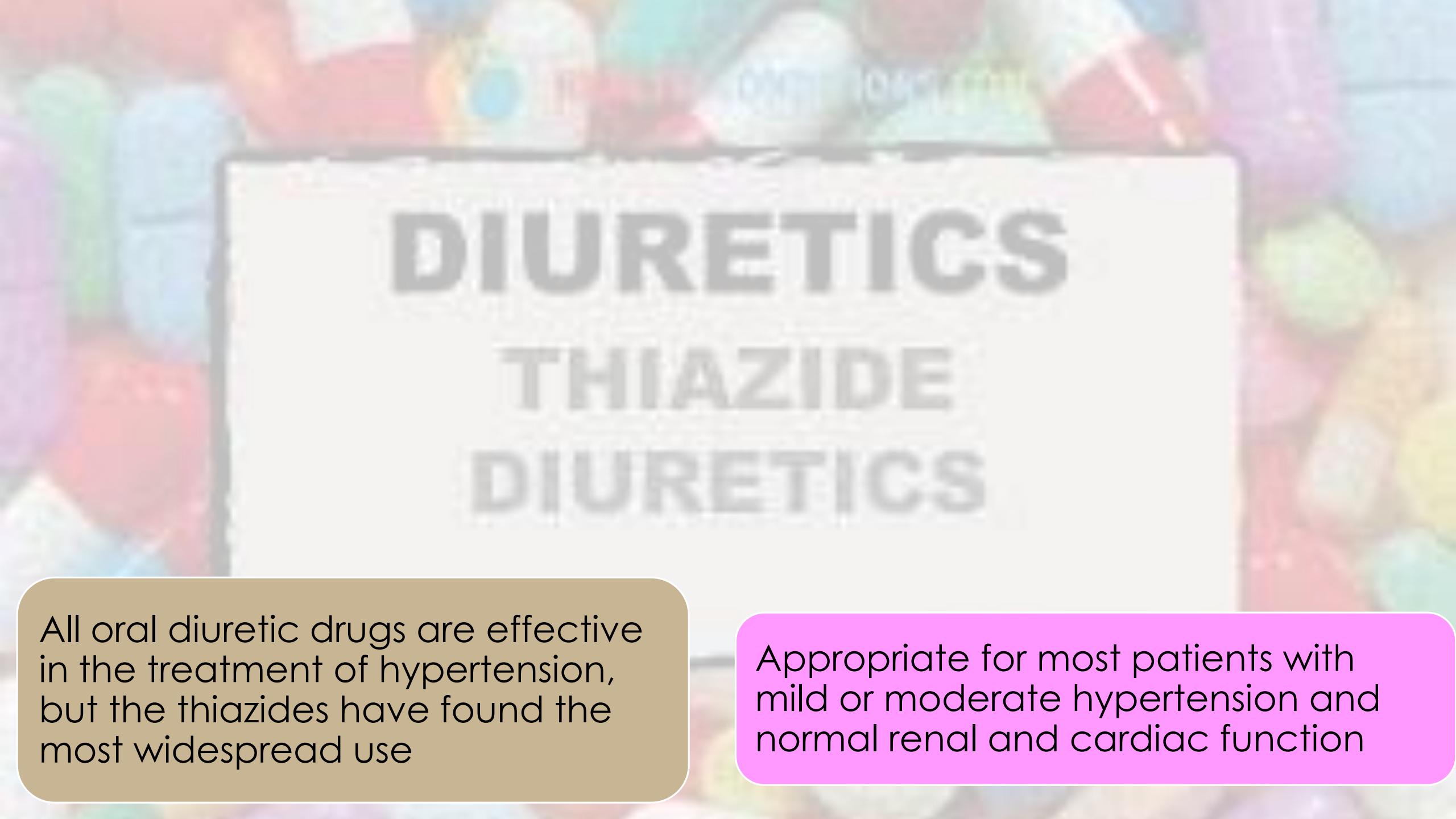
In more severe hypertension diuretics are used in combination with sympathoplegic and vasodilator drugs to control the tendency towards sodium retention caused by these agents.

CLASSIFICATION

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DIURETICS





DIURETICS

THIAZIDE

DIURETICS

All oral diuretic drugs are effective in the treatment of hypertension, but the thiazides have found the most widespread use

Appropriate for most patients with mild or moderate hypertension and normal renal and cardiac function

Because the site of action of the thiazide derivatives is on the luminal membrane, these drugs must be excreted into the tubular lumen to be effective

Thiazide derivatives act mainly in the cortical region of the ascending loop of Henle and the distal tubule to decrease the reabsorption of Na^+ , apparently by inhibition of a Na^+/Cl^- -co-transporter on the luminal membrane of the tubules

Therefore, with decrease renal function, thiazide diuretics lose efficacy

As a result, these drugs increase the concentration of Na^+ and Cl^- in the tubular fluid

Pharmacokinetics of thiazides diuretics

1

Thiazides
are orally
active.

Absorption
and
elimination
rates vary
considerably

2

3

But no clear
advantage is
present for 1
drug over
another

- Hyperuricemia
- Hypokalemia
- Hypomagnesemia
- Hyperglycemia
- gout



- Major action on the ascending limb of the loop of Henle
- The loop diuretics are the most efficacious of the diuretic drugs,
- Because the ascending limb accounts for the reabsorption of 25 to 30 percent of filtered NaCl, and downstream sites are not able to compensate for this increased Na⁺ load.
- Furosemide is the most commonly used of these drugs.

LOOP DIURETICS

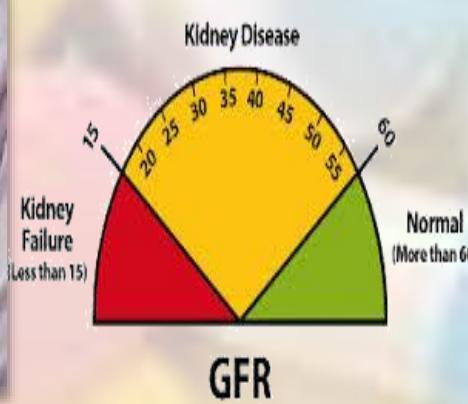


Loop diuretics are necessary:

in severe hypertension, when multiple drugs with sodium retaining properties are used

When GFR is less than 30 or 40ml/min

In cardiac failure or cirrhosis, in which sodium retention is marked



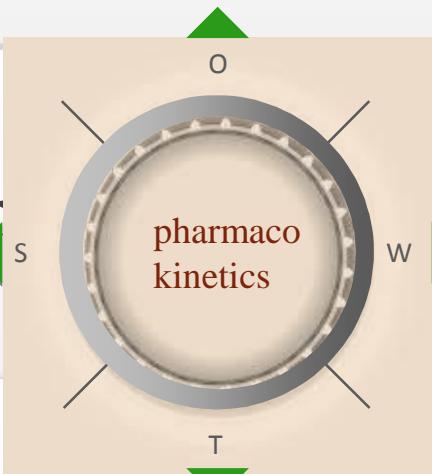
Absorption

Distribution

Excretion

Administration
Are adm orally or parentrally

Elimination
Eliminated by urine



Duration
Duration is brief,
2-4 hrs.

Dosage
Furosemide: 20-80
torsemide: 2.5-20 mg
Bumetanide: 0.5-2mg



Ototoxicity

Hypokalemia

Hypovolemia

hyperuricemia



K-sparing diuretics act on the collecting tubule to inhibit Na⁺ reabsorption and K⁺ excretion

Major use is in the treatment of hypertension, most often in combination with a thiazide.

DIURETICS POTASSIUM SPARING DIURETICS

It is extremely important that patients treated with any potassium-sparing diuretic be closely monitored for potassium levels

Classification

POTASSIUM SPARING
DIURETICS

DIRECT ACTING
ALDOSTERONE
ANTAGONISTS

SPIRONOLACTONE

EPLERENONE

SODIUM INFLUX INHIBITORS

TRIAMTERENE

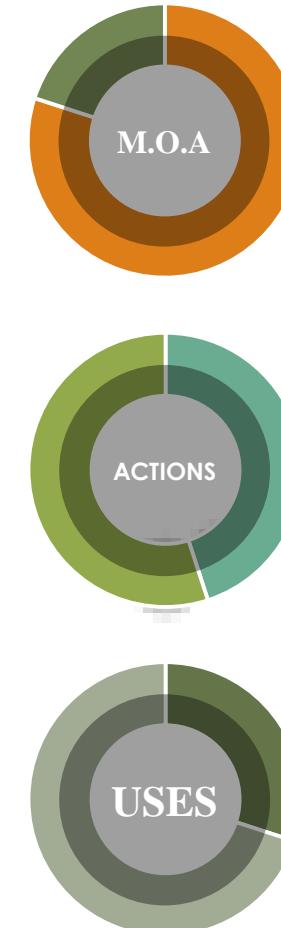
AMILORIDE

ALDOSTERONE ANTAGONISTS

SPIRONOLACTONE

EPLERENONE

Eplerenone



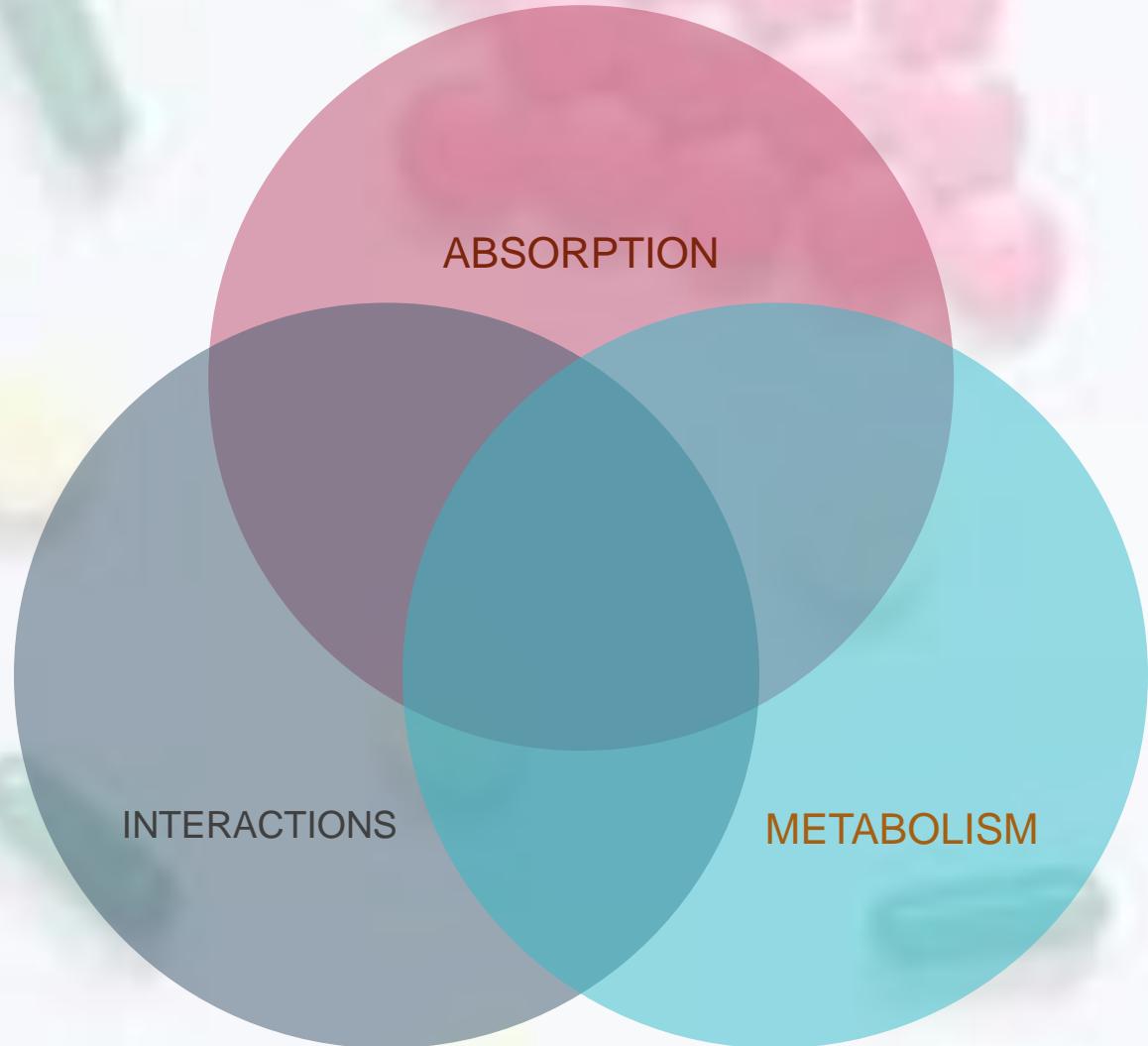
Diuretics prevent K secretion by antagonizing the effects of aldosterone at the late distal and cortical collecting tubules

When spironolactone is given to a patient with elevated circulating levels of aldosterone, the drug antagonizes the activity of the hormone, resulting in retention of K⁺ and excretion of Na⁺

Major use is in the treatment of hypertension, most common in combination with a thiazide diuretic

Spironolactone

SPIRONOLACTONE



Spironolactone is completely absorbed orally and is strongly bound to proteins

It is rapidly converted to an active metabolite, canrenone.
The action of spironolactone is largely due to the effect of canrenone, which has mineralocorticoid-blocking activity

Spironolactone induces hepatic cytochrome P450.

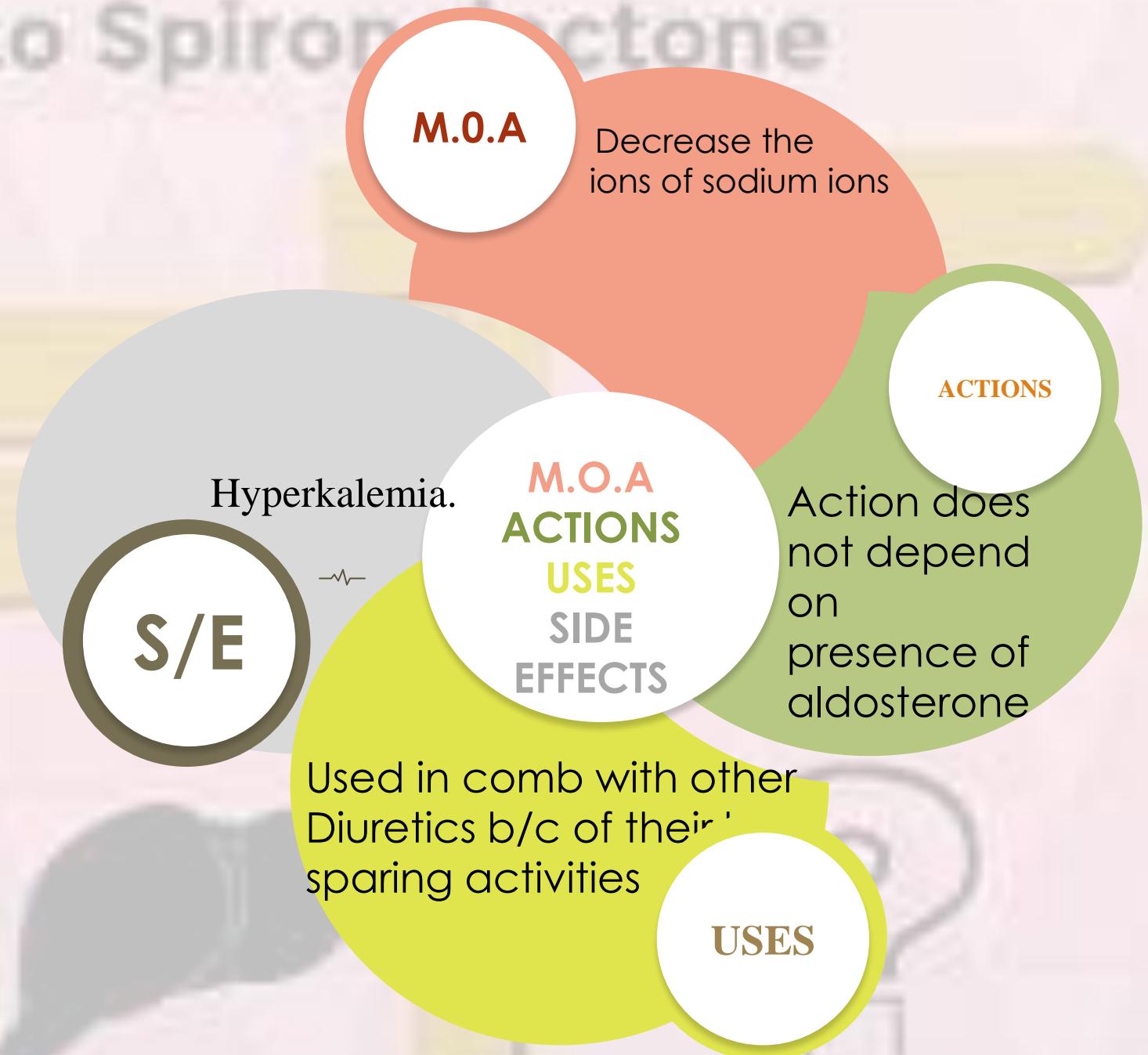


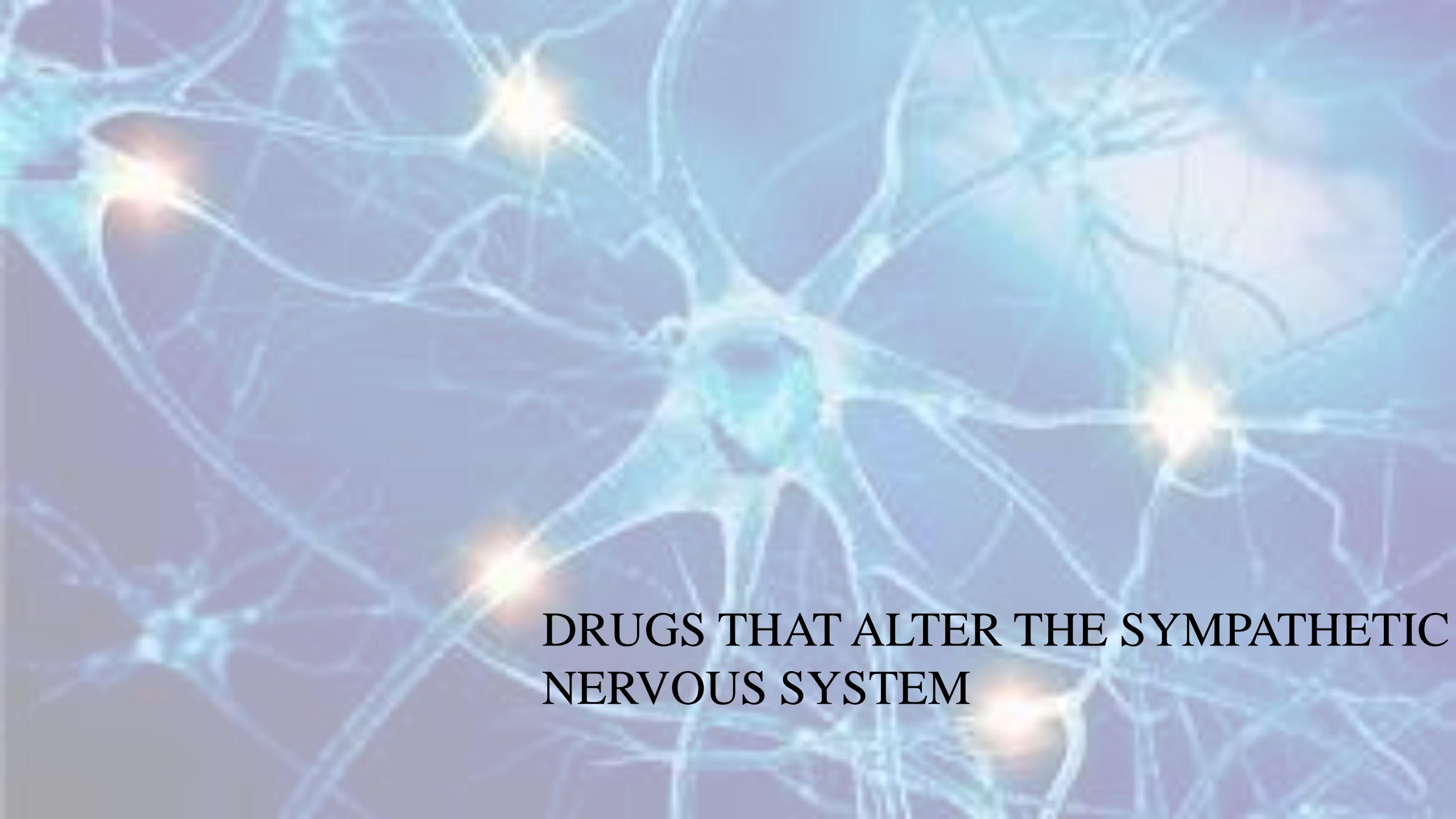
HYPERKALEMIA

Alternatives to Spironolactone

NA- INFLUX INHIBITORS

- TRIAMTERENE
- AMILORIDE

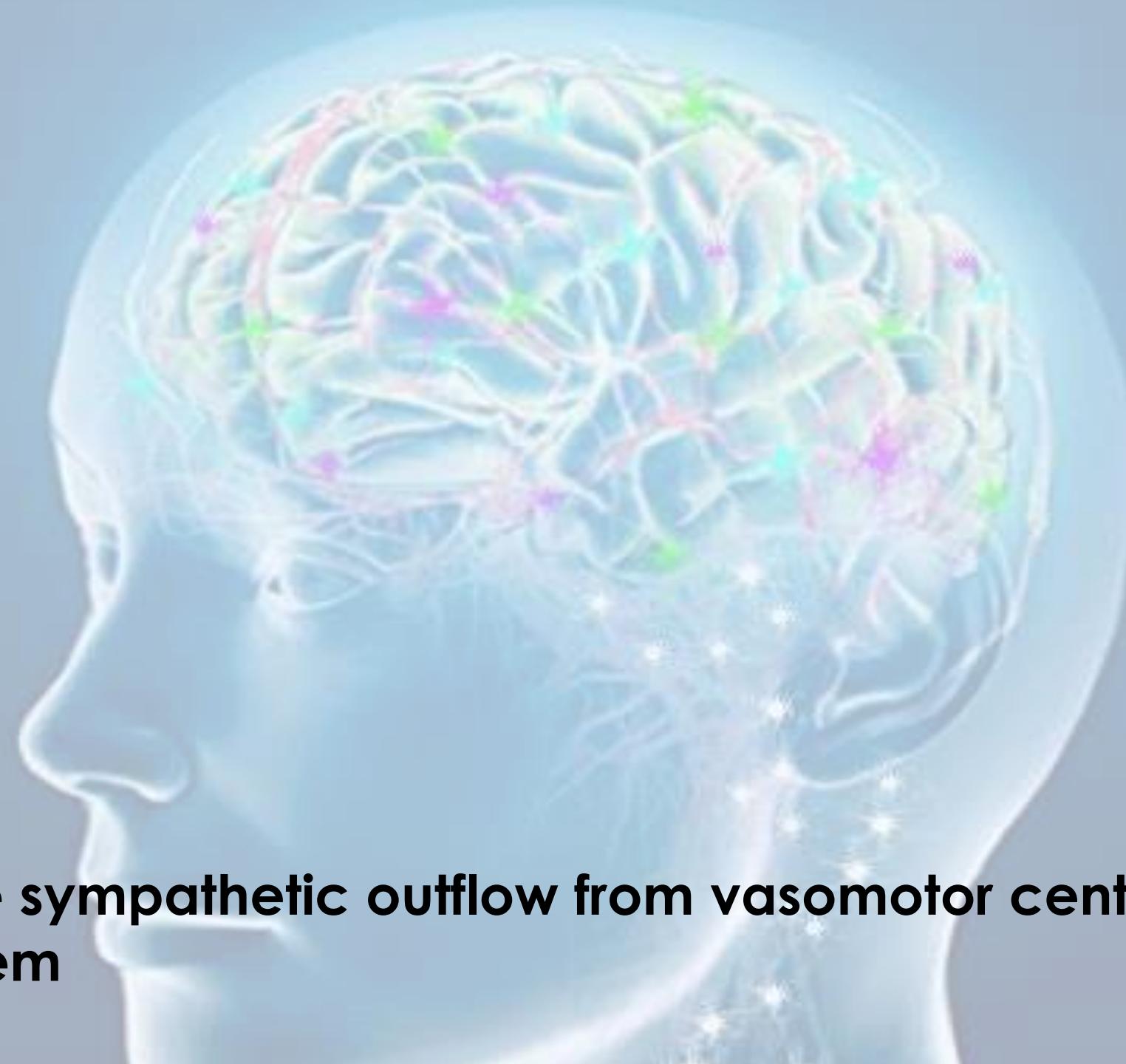




DRUGS THAT ALTER THE SYMPATHETIC NERVOUS SYSTEM



CENTRALLY ACTING SYMPATHOPLEGIC DRUGS



Reduce sympathetic outflow from vasomotor centers in the brainstem



CLONIDINE

DRUGS

METHYLDOPA

CLONIDINE

MOA

This α_2 -agonist diminishes the central adrenergic outflow, decreasing the firing rate of the sympathetic nerves and the amount of norepinephrine release

USES

primarily for the treatment of hypertension that has not responded adequately to treatment with two or more drugs

PKs

absorbed well after oral administration and is excreted by the kidney



- ✓ Sedation
- ✓ Dry mouth
- ✓ Constipation
- ✓ Rebound htn occurs upon sudden withdrawal of clonidine



VERTIGO

IMPAIRED CONC

SEDATION

NIGHTMARES

DEPRESSION

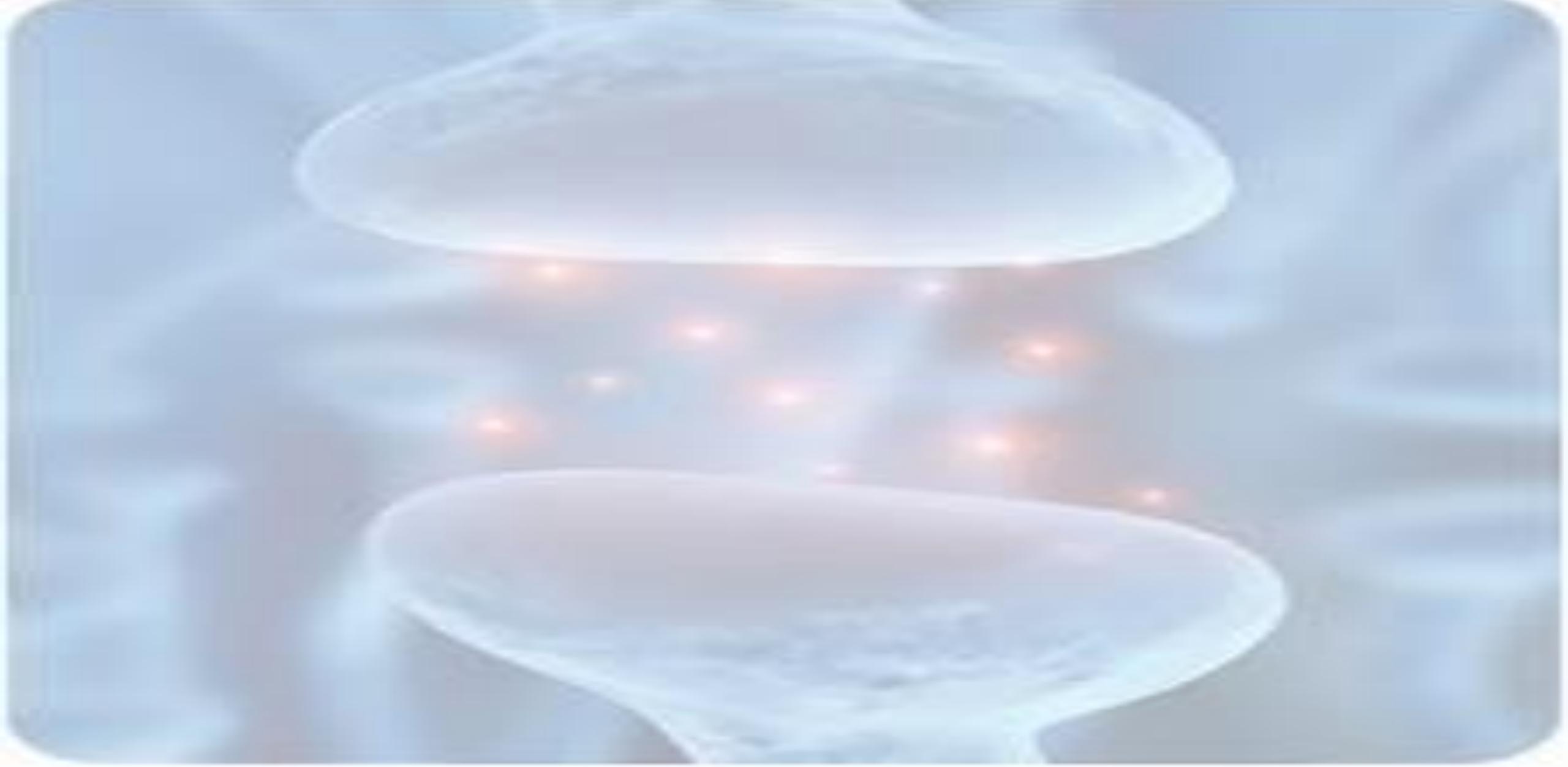




ADRENERGIC NEURON BLOCKING AGENTS

MECHANISM OF ACTION

These drugs lower b.p by preventing normal physiologic release of norepinephrine from postganglionic sympathetic neurons



GUANETHIDINE

DRUGS

RESERPINE

SIDE EFFECTS

- Diarrhoea
- Orthostatic hypotension



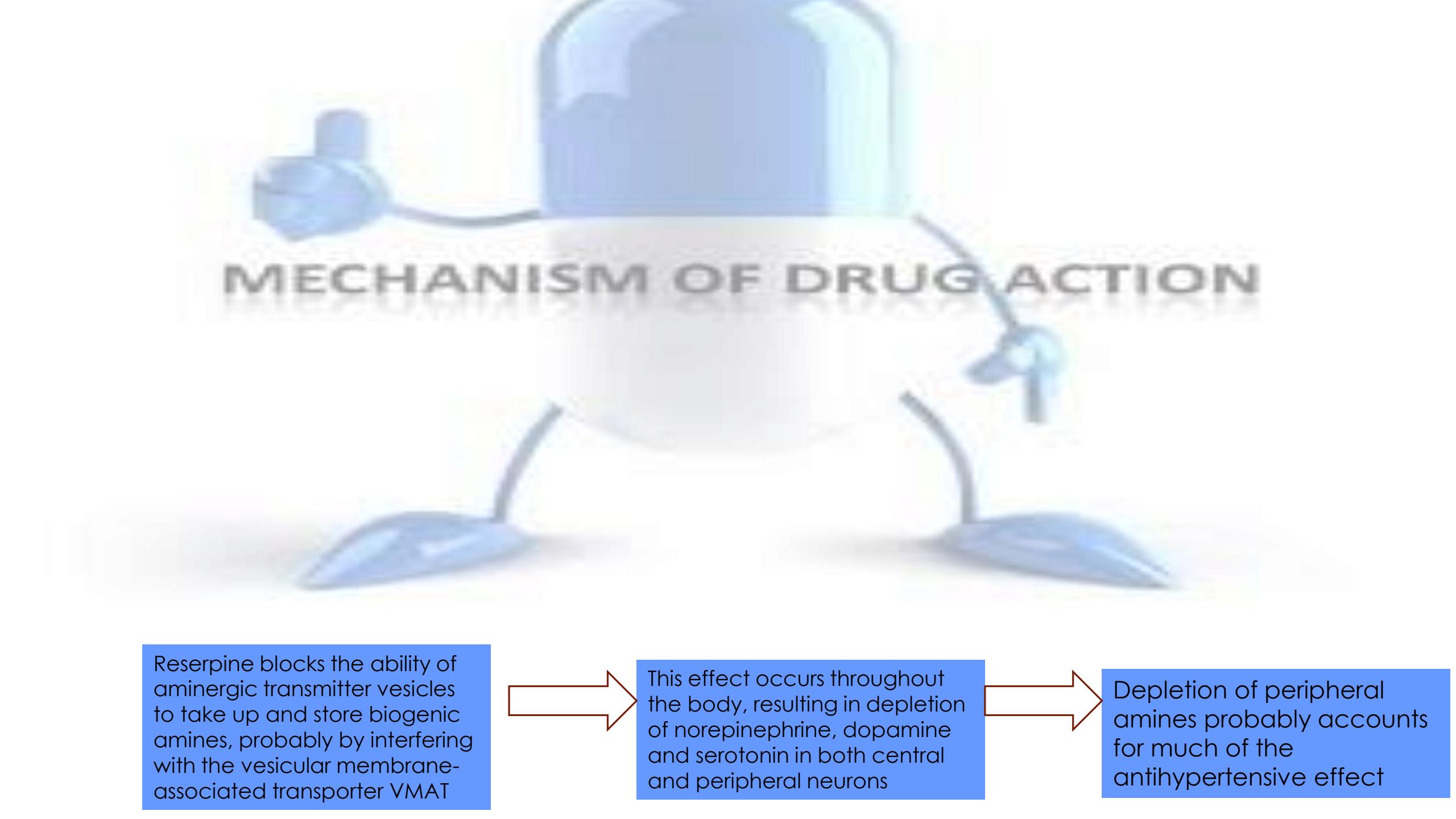
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ORIGIN
Rauwolfia

RESERPINE

- An alkaloid extracted from the roots of an Indian plant, ‘*Rauwolfia serpentina*’.
- It was one of the first effective drugs used on a large scale in treatment of hypertension.
- At present, it is rarely used owing to its adverse effects



MECHANISM OF DRUG ACTION

Reserpine blocks the ability of aminergic transmitter vesicles to take up and store biogenic amines, probably by interfering with the vesicular membrane-associated transporter VMAT



This effect occurs throughout the body, resulting in depletion of norepinephrine, dopamine and serotonin in both central and peripheral neurons



Depletion of peripheral amines probably accounts for much of the antihypertensive effect



SEDATION



DEPRESSION



NIGHTMARES



ADRENERGIC RECEPTOR ANTAGONISTS

CLASSIFICATION

BETA
BLOCKERS

ALPHA
BLOCKERS

ALPHA/BETA
BLOCKERS



BETA BLOCKERS

SELECTIVE VS NON-SELECTIVE BETA BLOCKERS

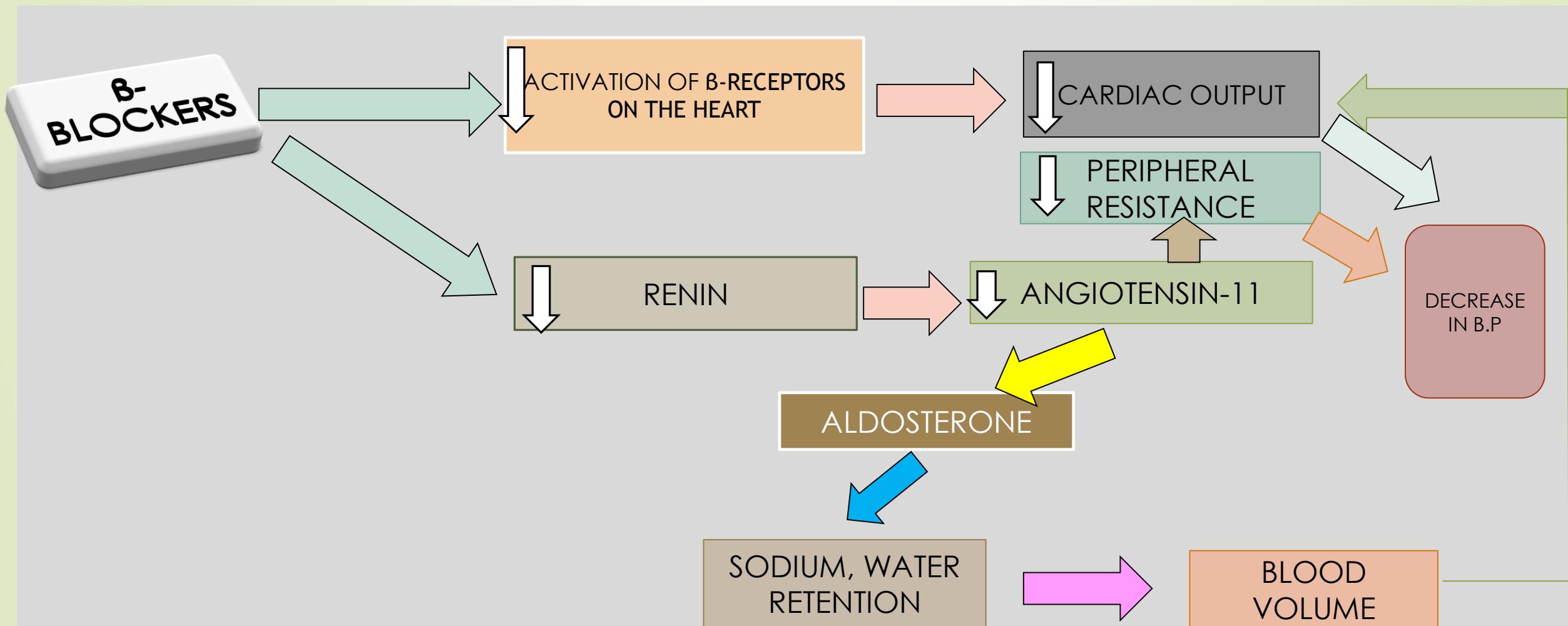
SELECTIVE

ATENOLOL
METOPROLOL
BISOPROLOL
ESMOLOL
NEBIVOLOL
BETAXOLOL

NON- SELECTIVE

PROPRANOLOL
PINDOLOL
NADOLOL
CARTEOLOL
ACEBUTOLOL
PENBUTOLOL

ACTIONS OF β -ADRENOCEPTOR BLOCKING AGENTS





Side Effects

- ❖ Principal toxicities result from blockade of cardiac, bronchial β -receptors

PINDOLOL, ACEBUTOLOL AND CARVEDILOL

They are partial agonists, ie, beta blockers with some intrinsic sympathomimetic activity.

Lower b.p by decreasing vascular resistance and appear to depress cardiac output or heart rate less than other beta blockers perhaps b/c of significantly greater agonist than antagonist effects at beta 2 receptors



ALPHA/BETA ADRENERGIC ANTAGONISTS

LABETOLOL AND CARVEDILOL

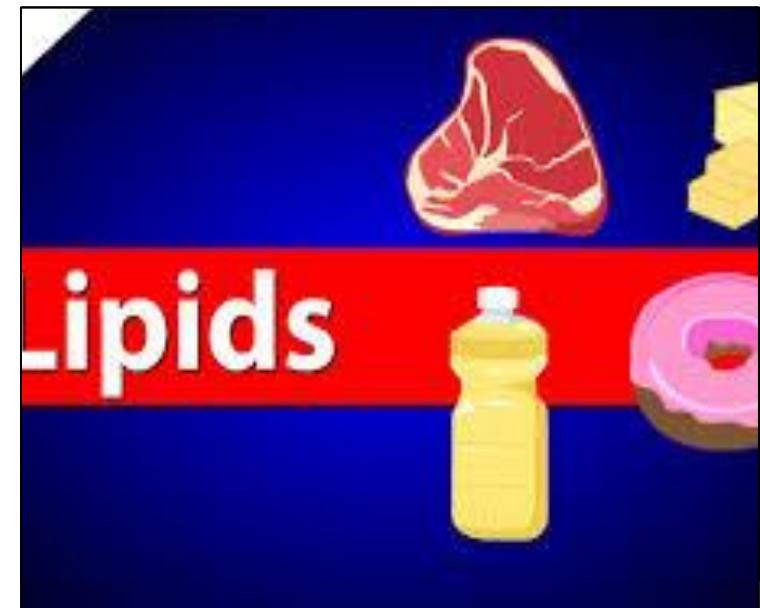
- ❖ These drugs have both β blocking and vasodilating effects.
- ❖ Because of its combined α β blocking activity, labetolol is useful in treating the hypertension of pheochromocytoma and hypertensive emergencies

ESMOLOL

- Used for management of intraoperative and postoperative hypertension
- Sometimes for hypertensive emergencies, particularly when hypertension is associated with tachycardia

Beta Blocker Toxicity

- Bradycardia
- Fatigue
- Lethargy
- Disturb lipid metabolism



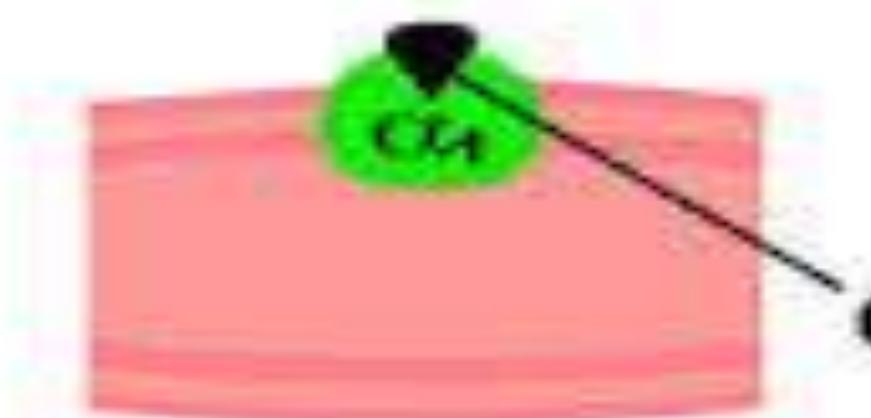


**ALPHA ADRENOCEPTOR
ANTAGONISTS**



α_1 Adrenoceptors

Alpha-1 blockers occupy alpha-1 receptor sites for norepinephrine and so inhibit smooth muscle contraction



α_1 Blocker

MECHANISM OF ACTION

CLASSIFICATION

SELECTIVE α_1 -BLOCKERS

- ▶ DOXAZOSIN
- ▶ PRAZOSIN
- ▶ TERAZOSIN



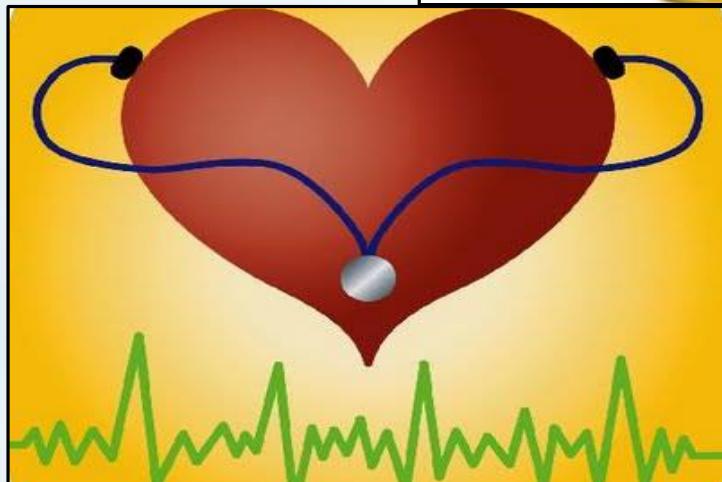
NON-SELECTIVE α -BLOCKERS

- ▶ PHENTOLAMINE
- ▶ PHENOXYBENZAMINE

DIZZINESS



PALPITATIONS



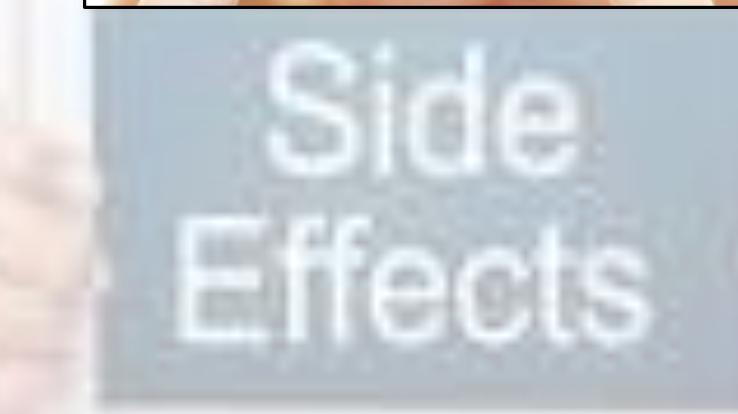
HEADACHE

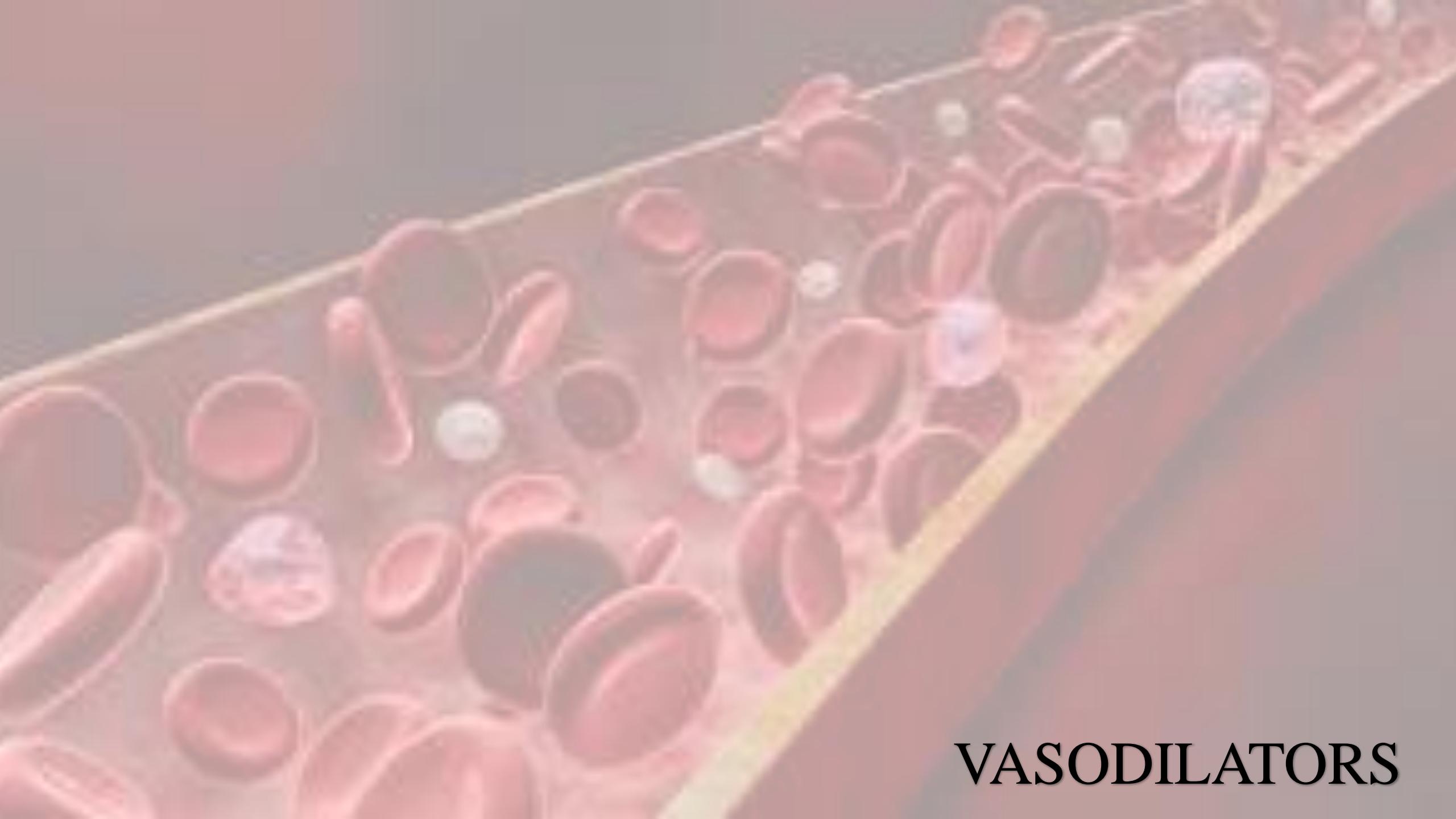


LASSITUDE



REFLEX TACHYCARDIA



A detailed, high-magnification micrograph of a blood vessel's tunica media. The image shows several layers of smooth muscle cells, each containing a prominent central nucleus. Interspersed between these layers are thick, yellowish elastic fibers that provide structural support. The overall texture is organized and layered.

VASODILATORS

Normal Blood Vessel



Dilated Blood Vessel



Vasodilation

- Increased transport of O_2
- Nutrients
- Glucose
- Decreased blood pressure
- Removal of cellular waste products

Relax smooth muscles of arterioles, thereby decreasing systemic vascular resistance

VASODILATORS

NITROPRUSSIDE,
HYDRALAZINE,
NITRATES

MINOXIDIL
DIAZOXIDE

FENOLDOPAM

Release of
nitric oxide

Hyperpolarization of
smooth muscle
membrane through
opening of K-
channels

Activation of
dopamine
receptors

HYDRALAZINE AND SODIUM NITROPRUSSIDE

HYDRALAZINE

- Dilates arterioles but not veins.
- Combination of hydralazine with nitrates is effective in patients with both hypertension and heart failure

SODIUM NITROPRUSSIDE

Powerful parenterally adm vasodilator used in treating hyp emergencies as well as severe heart failure.

Both arteriolar and venodilator.

This action occurs as a result of activation of guanylyl cyclase,either via release of nitric oxide or by direct stimulation of the enzyme.

The result is increased intracellular cGMP, which relaxes vascular smooth muscle



Side Effects

HYDRALAZINE

- HEADACHE
- NAUSEA
- ANOREXIA
- PALPITATIONS
- SWEATING
- FLUSHING



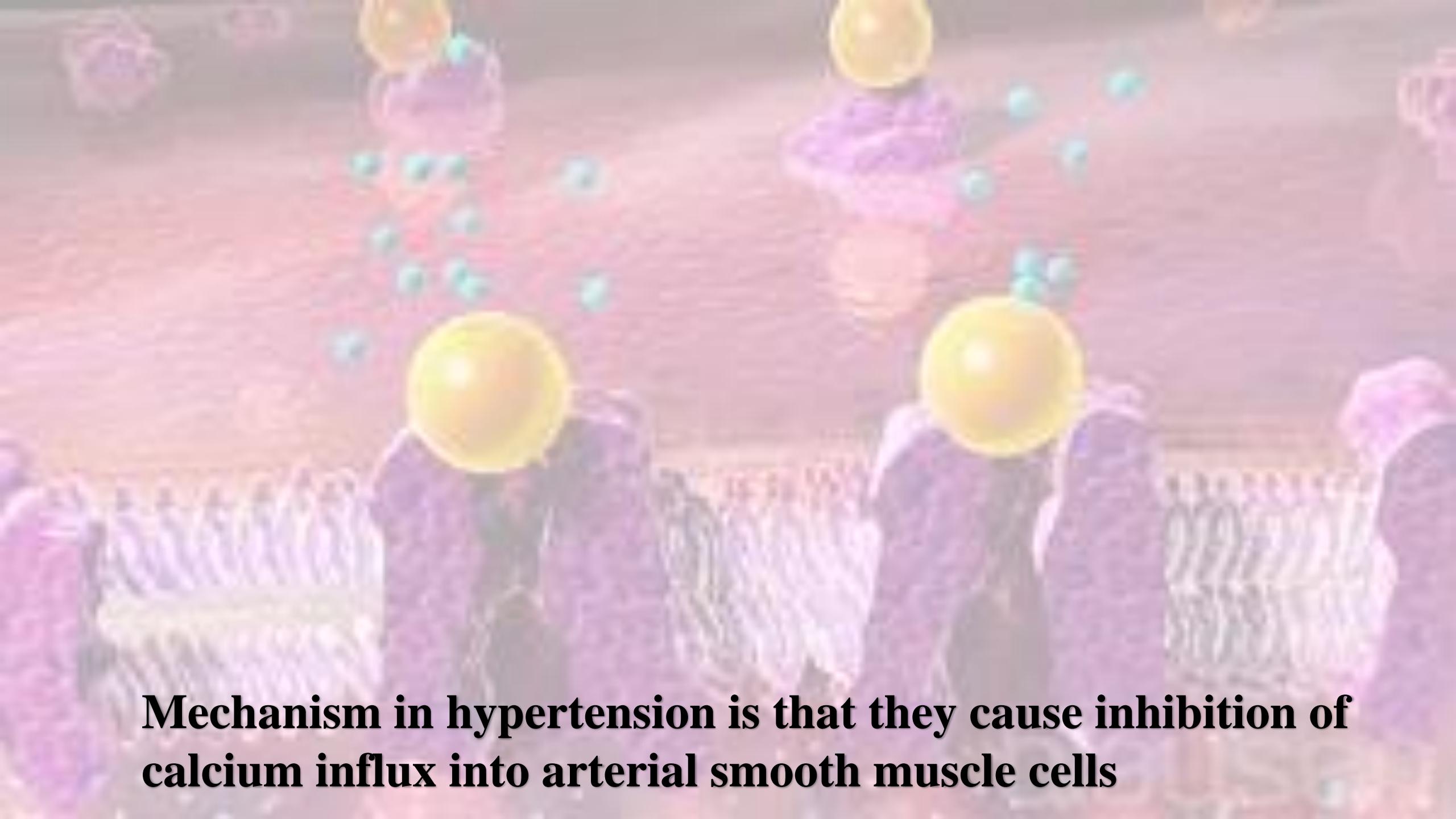
Na-NITROPRUSSIDE

- ARRHYTHMIAS
- METABOLIC ACIDOSIS
- EXCESSIVE HYPOTENSION





Calcium Channel Blockers



Mechanism in hypertension is that they cause inhibition of calcium influx into arterial smooth muscle cells

CLASSIFICATION

Dihydropyridines

Non-
dihydropyridines

DHPs

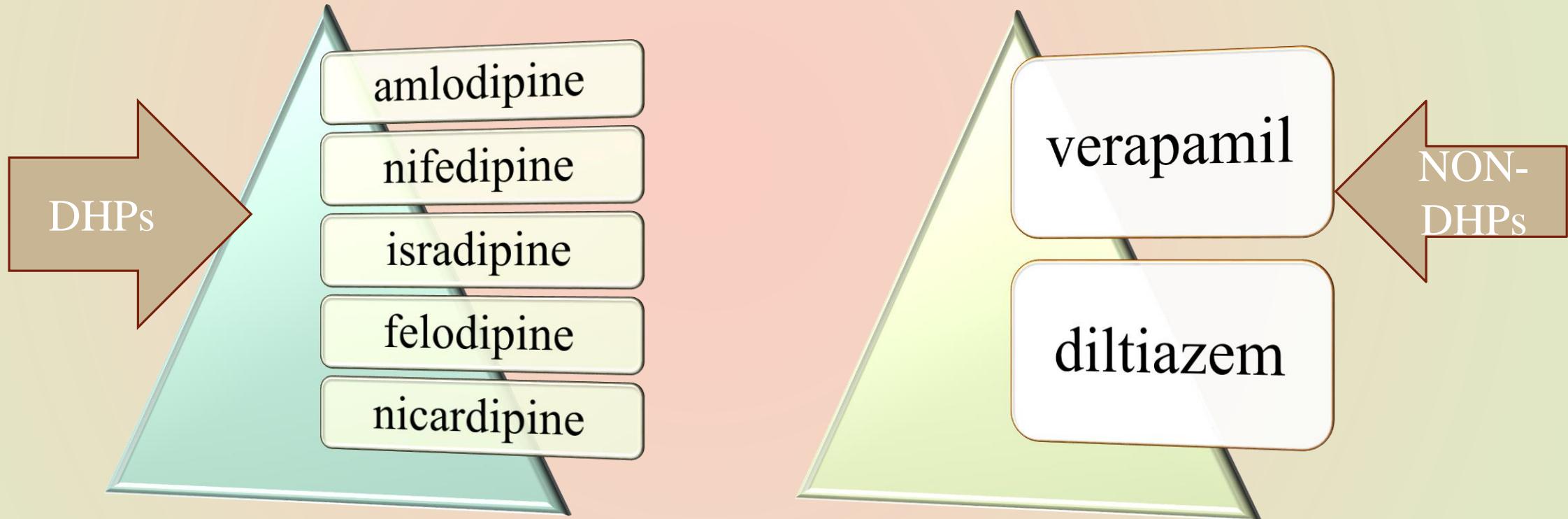
They exert an antihyp effect by causing peripheral vasodilation, without significantly affecting cardiac conduction and contractility.



NON-DHPs

They also have a modest antihyp effect but affect cardiac automaticity and conduction and hence are primarily used for management of arrhythmias

EXAMPLES OF DHPs AND NON-DHPs



Side Effects

CONSTIPATION

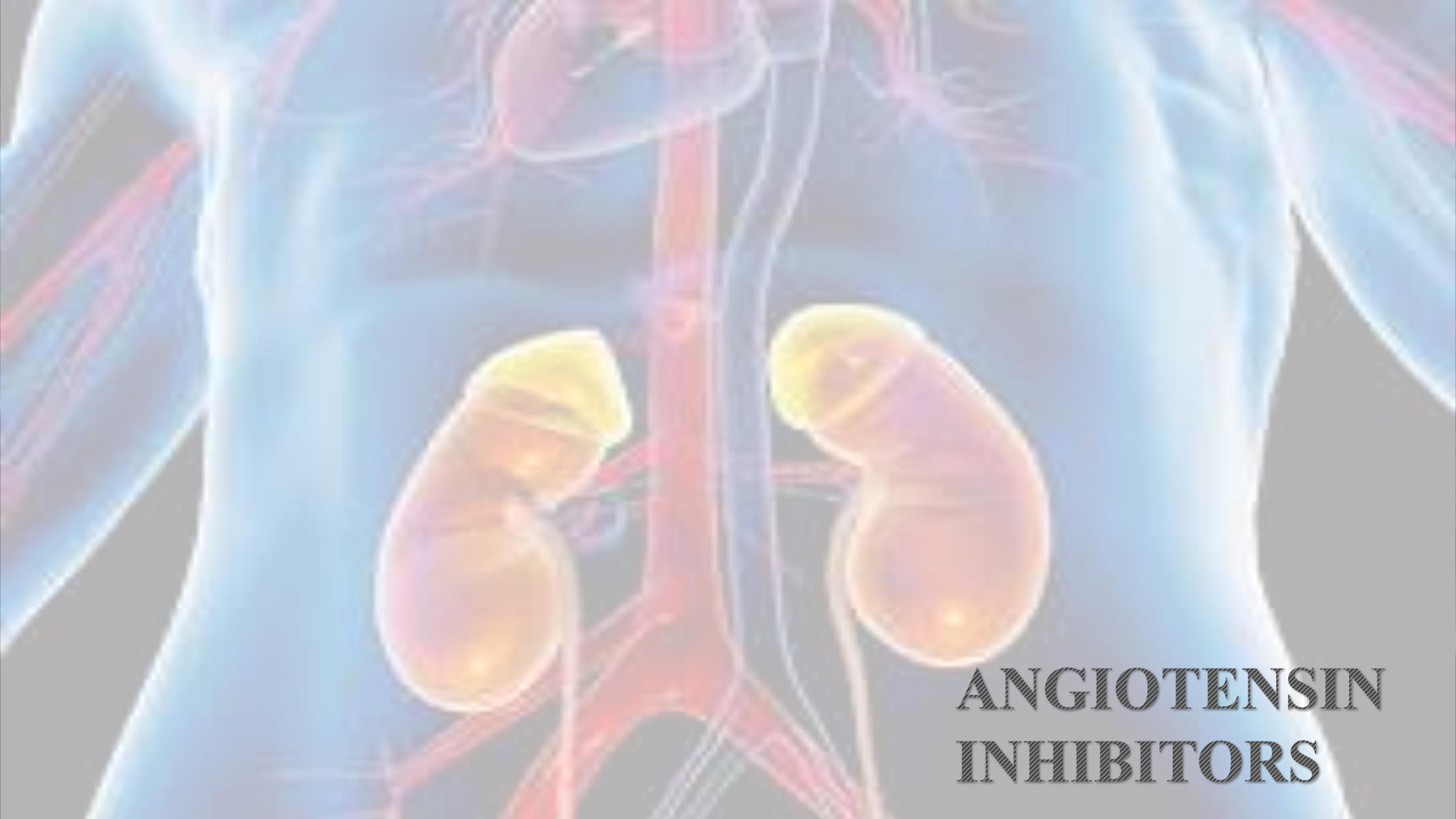
DIARRHOEA

HEADACHE

FEELING OF FATIGUE

GINGIVAL HYPERPLASIA





ANGIOTENSIN INHIBITORS

DRUGS ACTING ON RAAS

ALISKIREN

**ANGIOTENSIN CONVERTING
ENZYME INHIBITORS**

**ANGIOTENSIN
RECEPTOR BLOCKERS**





ACE Inhibitors

ACE INHIBITORS



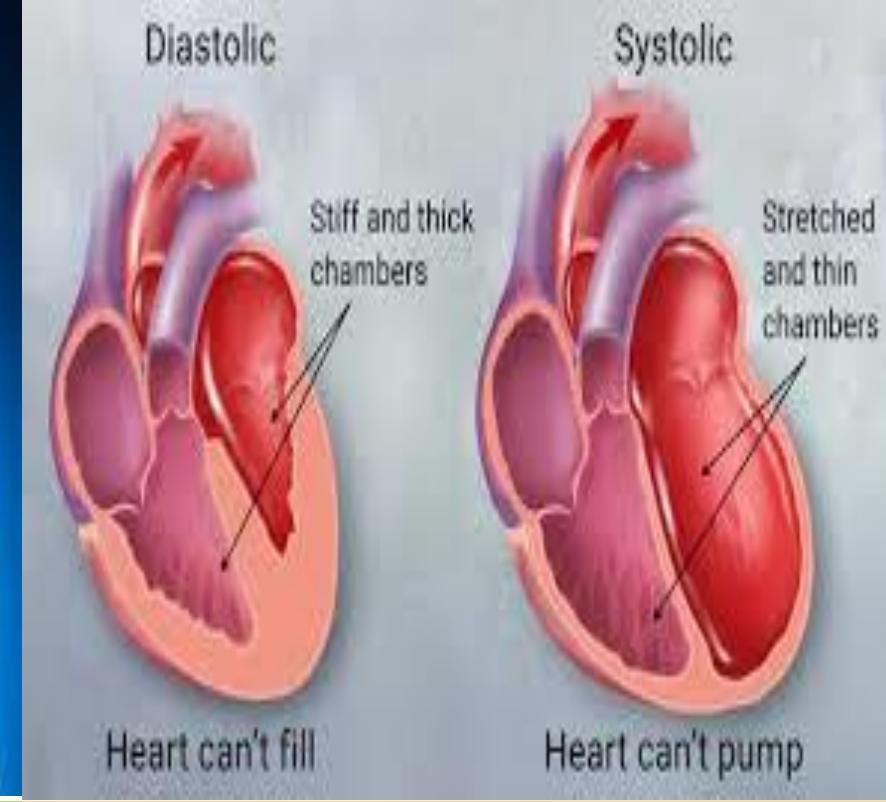
These drugs block the ACE that cleaves angiotensin I to form the potent vasoconstrictor angiotensin II

The converting enzyme is also responsible for the breakdown of bradykinin, which increases the production of nitric oxide and of prostacyclin by the blood vessels

Both nitric oxide and prostacyclin are potent vasodilators. ACE inhibitors decrease angiotensin II and increase bradykinin levels

Vasodilation of both arterioles and veins occurs as a result of the combined effects of lower vasoconstriction caused by diminished levels of angiotensin II and the potent vasodilating effect of increased bradykinin

By reducing circulating angiotensin II levels, ACE inhibitors also decrease the secretion of aldosterone, resulting in decreased sodium and water retention



useful role in treating pts with CKD because they diminish proteinuria and stabilize renal function

This effect is particularly effective in diabetes

Also proved to be useful in treatment of HF and after MI

THERAPEUTIC USES

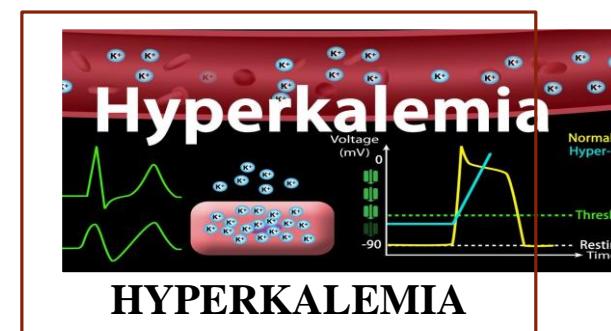
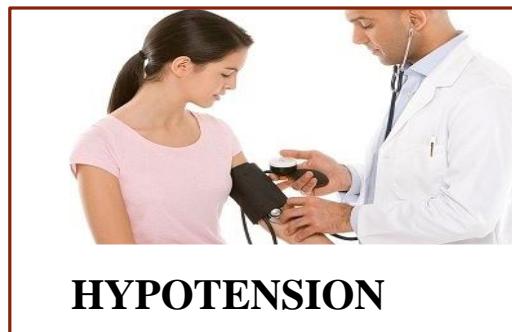
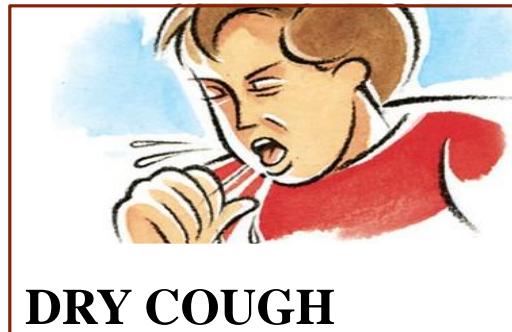
DRUGS

CAPTOPRIL

ENALEPRIL

LISINOPRIL

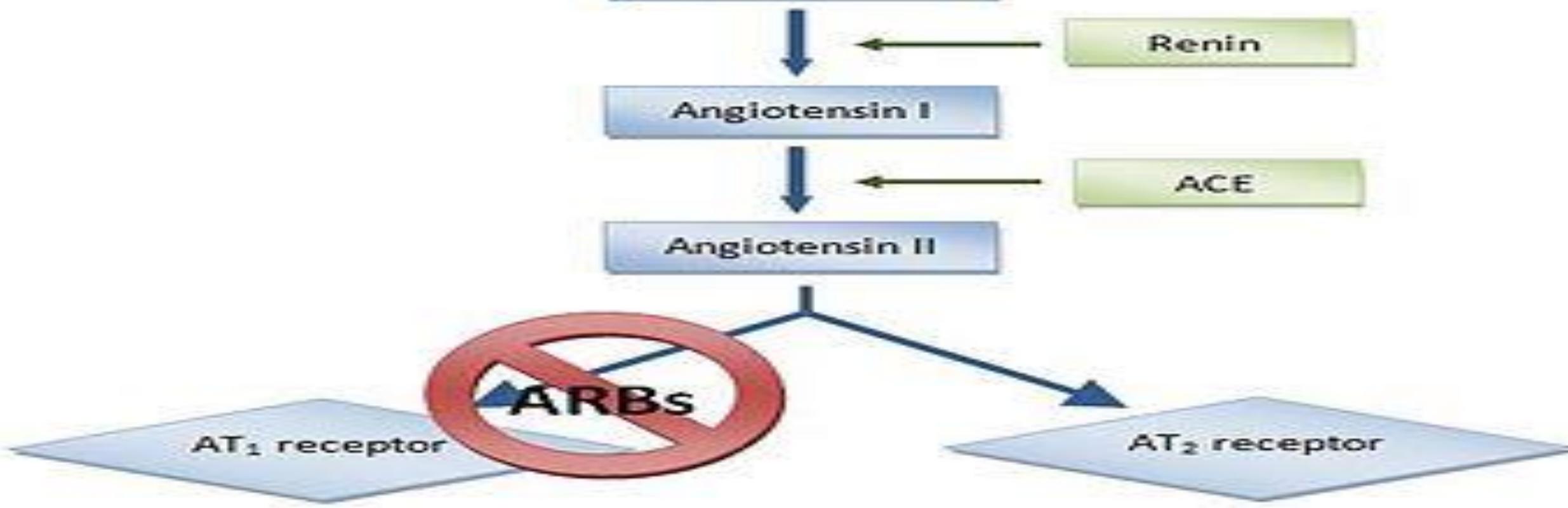
BENAZEPRIL



Angiotensin Receptor Blockers



ARBs

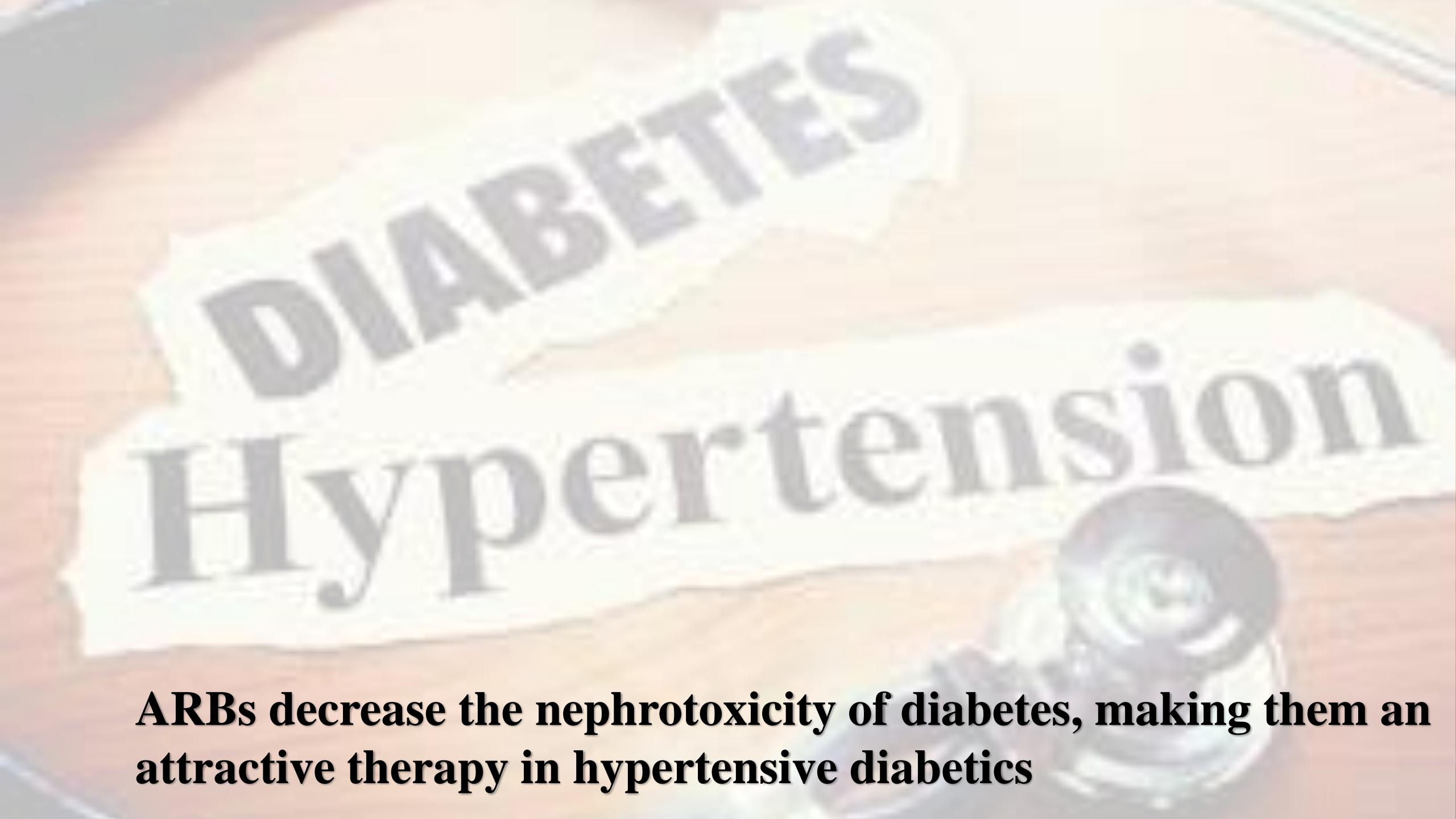


drugs block the AT1 receptors, decreasing the activation of AT1 receptors by angiotensin II

pharmacologic effects are similar to those of ACE inhibitors in that they produce arteriolar and venous dilation and block aldosterone secretion, thus lowering blood pressure and decreasing salt and water retention

ARBs do not increase bradykinin levels

Losartan is the prototypic ARB

A photograph of a book lying on a surface. The title 'DIABETES' is visible at the top, and 'Hypertension' is written vertically down the center of the cover. A magnifying glass is held over the bottom right corner of the book, focusing on the word 'Hypertension'.

DIABETES Hypertension

ARBs decrease the nephrotoxicity of diabetes, making them an attractive therapy in hypertensive diabetics



DRUGS

IRBESARTAN

LOSARTAN

CANDESARTAN

VALSARTAN

OLMESARTAN

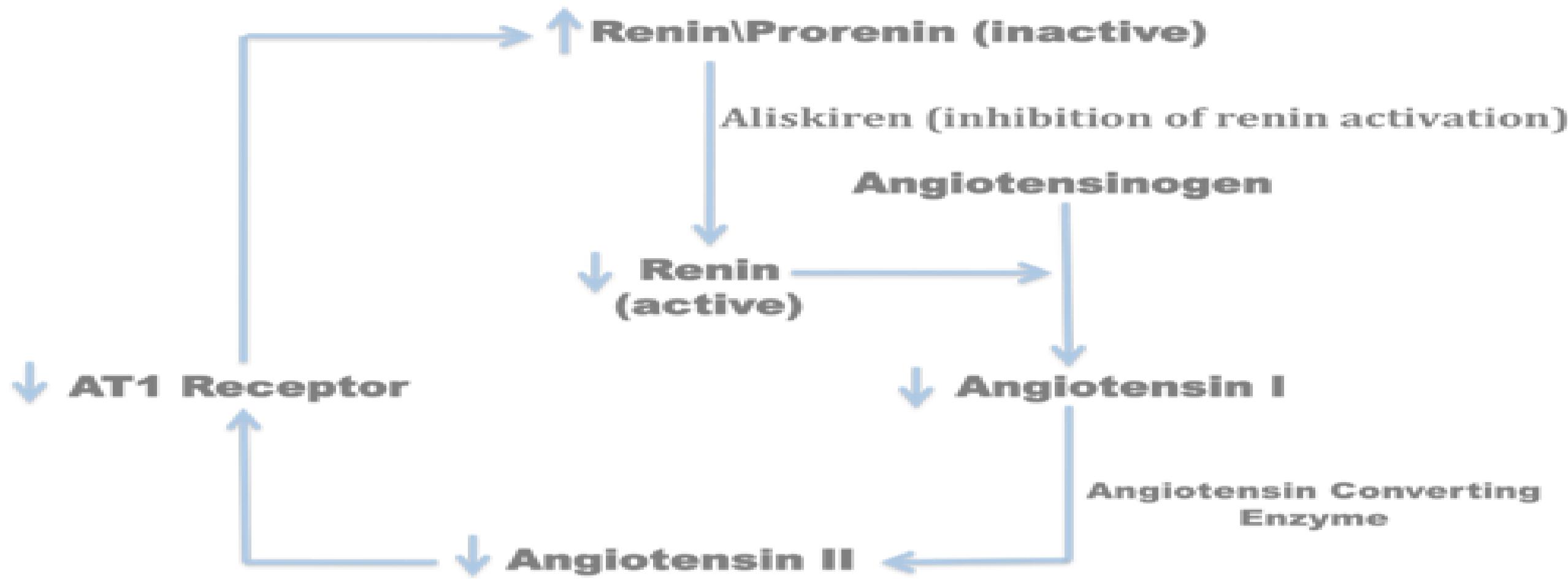
TELMISARTAN



Similar to ACEIs but risks of angioedema and cough is significantly decreased



**SELECTIVE RENIN
INHIBITOR(ALISKIREN)**



Aliskiren directly inhibits renin and, thus, acts earlier in the renin-angiotensin-aldosterone system than do ACE inhibitors or ARBs

It lowers blood pressure about as effectively as ARBs, ACE inhibitors, and thiazides

It can also be combined other antihypertensives, such as diuretics, ACE inhibitors, ARBs, and calcium-channel blockers



Side
Effects



Diarrhoea



Cough



Angioedema



HYPERTENSION EMERGENCY AND URGENCY

HTN EMERGENCY

BP elevation is associated with neurological, myocardial or renal TOD (target organ disease)



HTN URGENCY

Potential for TOD is great and likely to occur if BP is not controlled

MANAGEMENT OF HYPERTENSIVE EMERGENCY :

- ▶ Nitroprusside
- ▶ Fenoldopam
- ▶ nitroglycerin
- ▶ hydralazine

MANAGEMENT OF HYPERTENSIVE URGENCY

- ▶ Acute administration of short acting oral drug (captopril, clonidine or labetalol) followed by careful observation for several hours to ensure a gradual B.P reduction is an option.
- ▶ Oral captopril doses of 25-50 mg may be given at 1-2 hours interval . The onset of action is 15-30 minutes.
- ▶ Labetalol can be given in a dose of 200-400 mg followed by additional doses every 2-3 hours.



**Thank
You!!!**